

Remarks

Claims 1-8 and 32-43 are pending in this application. No amendments are made in this paper. No new matter has been introduced. Applicants respectfully submit that the pending claims are allowable for at least the following reasons.

A. The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn

On pages 2-3 of the Office Action, the rejection of claims 1-8 and 32-43 under 35 U.S.C. § 103, as allegedly obvious over Jeffery *et al.*, *J. Chem. Soc., Perkin Trans.*, 1: 2583-9 (1996) (“Jeffery”) and Fang *et al.*, *Tetrahedron: Asymmetry*, 10: 4477-4480 (1999) (“Fang”) is maintained. Applicants respectfully traverse this rejection.

Applicants respectfully point out that a *prima case* of obviousness cannot be established by Jeffery and Fang because: 1) Jeffery and Fang fail to teach or suggest all of the limitations of the pending claims; and 2) there would have been no motivation for those of ordinary skill in the art to make and use the claimed compounds because neither reference suggests the desirability of the claimed compounds. *See* Applicants’ Response filed January 18, 2005, incorporated herein by reference.

First, it is clear that Jeffery fail to teach the claimed compounds. To the extent that the Examiner relies on Compounds 4 and 5a of Jeffery, Applicants respectfully point out that those compounds are not encompassed by the pending claims as Compounds 4 and 5a disclosed Jeffery are not stereoisomers, as recited by the pending claims.¹ As Applicants repeatedly pointed out, while Compound 5a shows cis/trans isomerism, it does not show stereoisomerism of the compound. In other words, Jeffery is completely silent about the optical rotation properties of the compounds it discloses. Furthermore, even assuming, *arguendo*, Jeffery did somehow disclose the stereoisomerism of Compound 5a, Jeffery is not enabling because Jeffery does not disclose or suggest how to prepare the stereoisomers. *See, e.g., In re Hoeksema*, 399 F.2d 269, 274 (C.C.P.A. 1968) (holding that where a

¹ The Examiner disregards this apparent fact by simply asserting that “[t]he examiner disagrees.” Office Action, page 2. However, because the Examiner fails to provide any factual basis or reasoning “why” he disagrees with this fact, Applicants respectfully submit that the Examiner’s disregard of this fact is improper.

process for making the compound was not known, the mere naming of a compound, without more, cannot constitute a description of the compound).²

In addition, Jeffery does not suggest the claimed compounds because it discloses nothing about the claimed compounds, and thus would not have provided to those of ordinary skill in the art with any suggestion whatsoever regarding the claimed compounds. In fact, Jeffery actively teaches away from the claimed invention by providing that the pharmacological activity of sibutramine is “mediated *predominantly* by” two demethylated amines of sibutramine (Compounds 2 and 3), which are not encompassed by the pending claims.

Fang does not cure this deficiency because Fang also does not teach or suggest the claimed compounds. Fang merely discloses the enantiomers of sibutramine and desmethylsibutramine, none of which are encompassed by the pending claims. Thus, it is clear that Fang does not teach the claimed compounds. Further, Fang does not suggest the claimed compounds because it does not disclose that the methods disclosed therein may be used for the preparation of other compounds, much less for the compounds claimed herein. Therefore, the combination of Jeffery and Fang fails to teach or suggest all of the limitations of the pending claims. For this reason alone, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

In response, the Examiner states that he “does not understand applicants’ argument that Fang disclose[s] the preparation of enantiomers but is silent to their desirability, and none of the compounds are claimed herein.” Office Action, page 2. However, Applicants’ respectfully point out that the Examiner appears to have misinterpreted Applicants’ argument. Applicants’ point was that although Fang discloses the synthesis of enantiomers of sibutramine and its metabolite, which are not encompassed by the pending claims, it discloses nothing with regard to the desirability of enantiomers in general, much less the claimed enantiomers. *See*

² The Examiner states that this argument is irrelevant because the pending claims are not directed to the method of preparation of the compound. Office Action, page 2. However, Applicants’ point is that Jeffery, even if it suggested stereoisomer of Compound 5a, which Applicants again point out that it does not, would not have enabled those of ordinary skill in the art to make and use the compound because it does not provide the method of making that compound.

Applicants' Response of May 5, 2005, page 3. Therefore, Fang would not have suggested the claimed compounds to those of ordinary skill in the art.

Furthermore, there would have been no motivation to combine or modify Jeffery and Fang. It is well-established that the prior art references themselves must provide the motivation to combine or modify to establish a *prima facie* case of obviousness. *See Noelle*, 355 F.3d 1343, 1352 (Fed. Cir. 2004) ("the suggestion ... 'must be founded in the prior art, not in the applicant's disclosure.'" (quoting *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991))). However, neither Jeffery nor Fang provides the required motivation because there is no suggestion whatsoever in either references that combining the two references to make and use the claimed compounds would be advantageous.³

Despite this fact, the Examiner alleges that the suggestion is provided by Fang because "inasmuch as the preparation is there, the desirability is there too." Office Action, page 2. Applicants respectfully point out that this statement is based on the Examiner's misunderstanding of what Fang discloses. As Applicants pointed out, Fang does not disclose the preparation of the claimed compounds. Rather, Fang discloses the preparation of compounds that are not encompassed by the pending claims. Further, Fang does not provide anything regarding whether the claimed compounds are useful. Combining this fact with Jeffery's disclosure that pharmacological activity of sibutramine predominantly comes from its metabolites that are not encompassed by the pending claims, it is clear that little motivation to combine or modify these two references would have existed.

Finally, the Examiner maintains his allegation that "it would have been obvious ... to obtain compounds of Jeffery et al having hydroxy substituents in different positions, and obtain enantiomers using the process of ... Fang et al," based on his allegation that "positional isomers are *prima facie* obvious." Office Action of February 9, 2005, page 3. Applicants respectfully disagree with the blanket statement that "positional isomers are *prima facie* obvious," because each obviousness determination should rest on its own facts. *See, e.g., In re Grabiak*, 769 F.2d 729, 731

³ Indeed, Applicants respectfully point out that even if the two references are combined, those of ordinary skill in the art would not have arrived at the present invention because the combination fails to teach or suggest all of the claim limitations, as discussed above.

(Fed. Cir. 1985) (“Generalization should be avoided insofar as specific chemical structures are alleged to be prima facie obvious one from another.”). Thus, *prima facie* obviousness of a claimed compound cannot be established if its assertion is based on nothing more than a structural similarity between the claimed compound and those in the prior art. *See, e.g., Yamanouci Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000) (“a prima facie case of obviousness requires structural similarity between claimed and prior art subject matter ... where the prior art gives reason or motivation to make the claimed compositions .”) (emphasis added).

Accordingly, the question is whether those of ordinary skill in the art would have been motivated to make and use the claimed invention, not whether such persons could have made the claimed invention. *See In re Mills*, 916 F.2d 680, 682 (Fed. Cir. 1990) (holding that the mere fact that prior art references can be combined or modified does not render the combination obvious unless the prior art also suggests the desirability of the combination). As discussed above, neither Jeffery nor Fang suggests the desirability of the claimed invention, and the Examiner does not provide any evidence to the contrary. Indeed, Jeffery discourages those of ordinary skill in the art from making and using the claimed invention. Consequently, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

Conclusion

For at least the foregoing reasons, Applicants respectfully submit that all of the pending claims are allowable, and request that rejections directed to the claims be withdrawn.

No fee is believed due for this submission. Should any additional fees be due for this submission or to avoid abandonment of the application, please charge such fees to Jones Day Deposit Account No. 503013.

Respectfully submitted,

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